538,234

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

09 JUN 2005

(43) International Publication Date
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number
WO 2004/052450 A1

(51) International Patent Classification[7]: A61N 1/36, 1/37, 1/368, 1/08

(21) International Application Number: PCT/TR2003/000092

(22) International Filing Date: 2 December 2003 (02.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2002/02651 12 December 2002 (12.12.2002) TR

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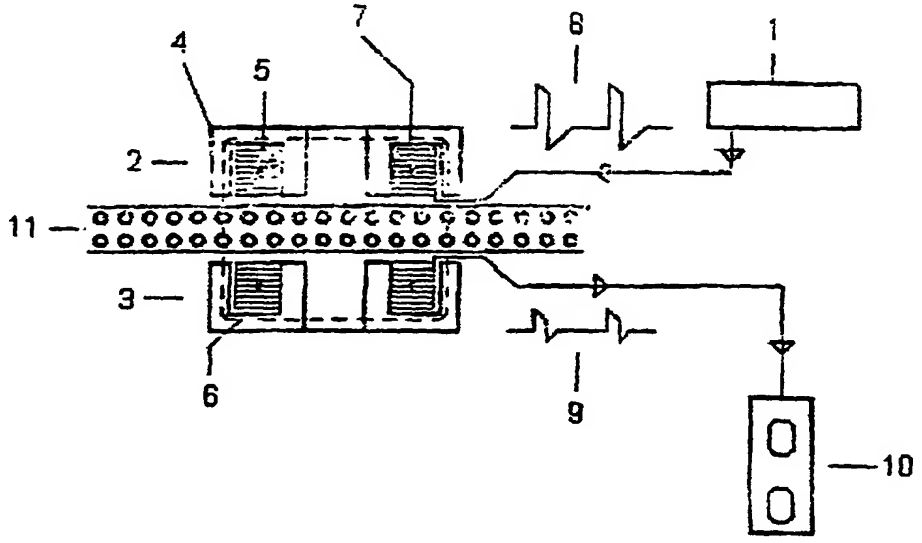
(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: EXTERNALLY ACTIVATED NEURO-IMPLANT WHICH DIRECTLY TRANSMITS THERAPEUTIC SIGNALS



(57) Abstract: We present here, an externally activated neuro-implant which dir ectly transmits terapeutic signals. It is an implantable device carrying out neurostimulation. It basicly consists of two coils. There are no electronic components in the internal part of system. The passive coil, that is implanted under the skin, is connected with the electrod in the epudural space of the spinal cord. The active coil is placed on the skin overlying the passive coil. Thrapeutic signals produced by the transmitter outside the body are directly transmitted by inductive coupling acroos the skin of the patient.

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EXTERNALLY ACTIVATED NEURO-IMPLANT WHICH DIRECTLY TRANSMITS THERAPEUTIC SIGNALS

Our innovation is related to an externally activated neuro-implant which directly transmits therapeutic signals. In the relevant medical literature, such devices are called neuro-implant. Neuro-implant is a device that electronically stimulates the nerves system. Neurostimulation is a process, by which nerves partially loosing their function as a result of disease or travma, are stimulated using artificial electrical pulses for regeneration (1). Electrical signals used for this purpose must be consistent with the natural activity of human neurophysiology [(2),(3),(4),(5)].

Implanted electrical stimulators were first used in 1967. They were primarily developed for the management of chronic pain (6). In the case of persistent and extensive pain, especially neurogenic pain that does not generally respond to drugs, transcutaneous stimulation is not adequate due to the need for multiple electrode placement and increased skin impedance. In order more effectively to cover the painful area, direct stimulation of the spinal cord is necessary via an implantable electrode system (7). With further clinical studies in thisfield, therapeutic effects of the method on other conditions such as peripheral vascular disease in the lower extremities that may lead to amputation and movement disorders with partial motor problems have been observed [(8),(9)].

At present, most of the implants are produced in United States, and mainly used in western countries, e.g. US, England, Germany, France, Spain, Italy, Holland, Belgium, Sweeden. The existing dorsal column stimulators generally operate using radio-frequency (RF) transmission (7). These devices have four components: transmitter, antenna, receiver, and electrodes. The transmitter and antenna are external components; the receiver and the electrodes are internal components that are implanted in the body by the surgeon. The transmitter, powered by a 9 volt battery, generates RF signals by which electrical impulses are carried. The frequency of carrier waves is about 2 MHz, chosen to minimize the possibility of interference from outside sources, including microwave ovens and amplitude modulated (AM) and frequency modulated (FM) radios. These radio-waves are relayed, via the external antenna, through the skin to the receiver. The passive receiver then translates these signals into electrical impulses and deliveres them to the electrodes on the dorsal horn via flexible, insulated stainless-steel wires [(10),(11),(12)]. There are totally implantable systems with long-life battery that evantually needs to be replaced by another surgical procedure at approximately 5 years intervals (7).

Captions to Figures:

Figure – 1. General view of the new neuro-implant system.

Figure – 2. General view of the passive coil.

Figure – 3. General view of the active coil.

Figure – 4. A schematic diagram illustrating the transmission of therapeutic pulses by inductive coupling through the skin.

Figure – 5. Circuit diagram of the transmitter which drives the active coil. "Circuit components has been described in section called <<Explanation of the Parts in Figures>>.

Figure – 6. Printed circuit board (pcb) that shows the placement of the electronic components of the transmitter (scale: 1/1).

Figure – 7. Enlarged pcb of the transmitter showing the location of components (scale: 2x1).

Figure – 8. A single pulse produced by the transmitter in all stimulation modes. Pulse shape: asymetric biphasic rectangular, pulse width: 200 μs (can be selected between 50 μs and 400 μs by changing value of resistor R5 in the transmitter circuit), amplitude: 80 V over 1 kΩ (80 mA).

Figure – 9. Pulse patterns produced by the transmitter when set for the conventional mode of stimulation. In this mode; continuous pulses are repeated at a constant frequency between 30 Hz and 100 Hz.

Figure – 10. Pulse patterns produced by the transmitter when set for the burst mode of stimulation. In this mode; 80 ms long trains of pulses with an internal frequency of 80 Hz are repeated 1.3 times a second, each train consisting of 7 pulses. The number of pulses in each train, internal frequency and repeatation rate of the trains can be selected as wanted by changing the values of the relevant components in the transmitter circuit.

Figure – 11. Pulse patterns produced by the transmitter when set for the frequency modulated stimulation. In this mode; continuous pulses fluctate between 110 Hz and 55 Hz over 60 ms, 1.3 times a second. Fast pulses (110 Hz) are slowed down (55 Hz), for a short period (90 ms) 1.3 times a second, and then they get faster again. The frequency of fast and slow pulses can be selected as wanted by changing the values of the relevant components in the transmitter circuit.

Figure – 12. The coils tested to select optimal size for the active and passive coils (from left to right, the first one is the active coil, and the others passive).

Figure – 13. Graphical representation of the vertical distance tests using active and passive coils.

Figure – 14. Graphical representation of the lateral distance tests using active and passive coils.

Figure – 15. Output of the passive coil (I) when the active coil is placed right on it.

Figure – 16. Output of the passive coil (I) when separated from the active coil by 5 mm thick pig skin.

Figure – 17. Output of the passive coil (II) when separated from the active coil by 5 mm thick pig skin.

Figure – 18. Output of the passive coil (I) operating at 37°C when the active coil is placed right on it.

Figure – 19. Output of a commercially available spinal cord stimulator implant (Medtronic, model: 3521) when separated from the transmitter aerial by a vertical distance of 5 mm). "Amplitude: 9 mA, pulse width: 200 μs, pulse shape: monophasic rectangular. This result shows that it includes direct current (DC) component which is not wanted during physical therapy".

Figure – 20. Output of a commercially available spinal cord stimulator implant (Avery, model: S-218) when separated from the transmitter aerial by a vertical distance of 5 mm). "Amplitude: 8 mA, pulse width: 200 μs, pulse shape: monophasic rectangular. This result shows that it includes direct current (DC) component which is not wanted during physical therapy".

Figure – 21. Technical drawings of the ferrite pot core used for the active coil (top view and cross section).

Figure – 22. Technical drawings of the coil former used for active coil (top view and cross section).

Figure – 23. Technical drawings showing the encapsulation of active coil (top view and cross section).

Figure – 24. Technical drawings of the ferrite pot core used for passive active coil (top view and cross section).

Figure – 25. Technical drawings of the coil former used for passive coil (top view and cross section).

Figure – 26. Technical drawings of the coil former for the active coil (top view and cross section).

Figure – 27. Technical drawings of the multi-contact (four contacts/three channel) version of the new implant (top view and front view).

Explanation of the Code Numbers We Used in the Figures to Make Our Innovation More Clear:

(1) Transmitter.

(2) Active coil.

(3) Passive coil.

(4) Ferrite pot core.

(5) 42 S.W.G. (standard wire gauge) enammaled copper wire.

(6) Magnetic flux.

(7) Current flowing in the coil.

(8) Therapeutic signal supplied by the transmitter device.

(9) Therapeutic signal induced at the output of passive coil.

(10) Miniature electrode implanted in epidural space of the spinal cord.

(11) Skin between active and passive coils.

(12) CMOS 556 double timer.

(13) CMOS 555 single timer.

(14) Slow signal output of the double timer.

(15) Fast signal output of the double timer.

(16) Reset terminal of the single timer.

(17) Connections of the stimülasyon modes selector switch.

(18) R1 (30 k 0.25 W metal film resistor).

(19) R2 (30 k 0.25 W metal film resistor).

(20) R3 (30 k 0.25 W metal film resistor).

(21) R4 (43 k 0.25 W metal film resistor).

(22) R5 (1.8 k 0.25 W metal film resistor).

(23) R6 (330 Ω 0.25 W metal film resistor).

(24) R7 (10 k lineer potantiometer).

(25) R8 (150 Ω 0.25 W metal film resistor).

(26) R9 (1 k metal film resistor).

(27) C1 (0.22 µF 35 V tantalum capacitor).

(28) C2 (10 µF 16 V tantalum capacitor).

(29) C3 (0.1 µF 35 V tantalum capacitor).

(30) C4 (0.1 µF 35 V tantalum capacitor).

(31) C5 (47 µF 16 V tantalum capacitor).

(32) C6 (1 µF 100 V minik electrolytic capacitor).

(33) D1 (1N4148 diode).

(34) D2 (1N4148 di0de).

(35) D3 (1N4148 diode).

(36) TRS (ZTX605 darlington transistor).

(37) TRF (8x1 amplification output transformer).

(38) MPR (mikro power regulator).

(39) 9 V direct current (D.C.) input from PP3 model battery.

(40) Output of therapeutic signal from the transmitter device.

(41) (41) · Indicator lamp (low current LED).

(42) Optional resistor in the transmitter circuit (short-circuit for neuro-implant, 5.1 Ω for

percutaneous stimülation, 1 Ω for TENS application).

(43) Graphic of the results of vertical distance tests with active and passive coils.

(44) Graphic of the results of vertical distance tests with active and passive coils.

(45) Graphic of the results of vertical distance tests with active and passive coils.

(46) Graphic of the results of vertical distance tests with active and passive coils.

(47) Graphic of the results of vertical distance tests with active and passive coils.

(48) Graphic of the results of lateral distance tests with active and passive coils.

(49) Graphic of the results of lateral distance tests with active and passive coils.

(50) Technical drawing of the active coil (top view).

(51) Technical drawing of the active coil (cross section).

(52) Ferrite pot core.

(53) Active coil.

(54) Output of the connector..

(55) Technical drawing of the coil former used for active coil.

(56) Technical drawing of the coil former used for active coil (cross section).

(57) 1x4 mm soldering terminals.

(58) Technical drawing that shows the encapsulation of active coil.

(59) Technical drawing that shows the encapsulation of active coil (cross section).

(60) Encapsulation with polyuretan.

(61) Active coil.

(62) Protective sprey on the surface.

(63) Technical drawing of the passive coil (top view).

(64) Technical drawing of the passive coil (cross section).

(65) Ferrite core.

(66) Coil.

(67) (67) Output of the coil..

(68) Technical drawing of the coil former used for passive coil –I (top view).

(69) Technical drawing of the coil former used for passive coil –I (cross section).

(70) Technical drawing of the coil former used for passive coil – II (top view).

(71) Technical drawing of the coil former used for passive coil-II (cross section).

(72) Technical drawing of the coil former used for passive coil (top view).

(73) Coil former.

(74) Output of the coil.

(75) Technical drawing that shows the top view of the encapsulation of passive coil.

(76) Technical drawing that shows the side view (I) of the encapsulation of passive coil.

(77) Technical drawing that shows the side view (II) of the encapsulation of passive coil.

(78) 0.75 mm thick silicone sheet on the base.

(79) Encapsulation with 1 mm thick medical grade silicone.

(80) Passive coil.

(81) Coil output wires.

(82) Connectors made from stainless steel tube with a diameter of 7.5 mm.

(83) Technical drawing that shows top view of three-channel version of the new implant.

(84) Technical drawing that shows the front view of three channel version of the new implant.

(85) 42 S.W.G. "standard wire gauge" enammeled copper wire.

(86) 1 mm distance between the passive coils.

(87) Encapsulation with 1 mm thick medical grade silicone.

(88) Passive coils.

(89) Connectors made from stainless steel tube with a diameter of 7.5 mm.

A fundamental requirement for successful spinal cord stimulation is to deliver and maintain effective stimulation to the appropriate segments of the cord; stimulation paraesthesia must cover completely the area of target neurons, and it must not trigger

unwanted segmental sensations. There have been many reports about the successful use of neuroimplantation, but there have also been complaints about the performance of implanted stimulators, some of which relate to surgical technique. The problems encountered with the present implantable stimulator systems can be classified as follows (13): 1) Breakdown in the electronic components: The existing systems rely on the implantation of a receiver circuit which include electronic components and, as component failure is not unknown, patients can be subjected to further surgery to replace a defective receiver. 2) Fixed electrical parameters: majority of the existing systems, once implanted, generate a fixed electrical output preset by the manufacturers. The stimulation mode is of a conventional type that composes of pulses with constant frequency preset by the manufacturer (Figure – 9). Some of the most sophisticated systems do allow variations of some parameters, but this facility is both limited and expensive. 3) Electrode position: during the operation the electrode may be misplaced or, following the operation, electrodes may migrate, thus reducing the efficacy of the stimulation [(14),(15)]. Multi-contact electrodes have recently been produced to solve this problem (16). 4) The expense of the equipment: The high cost of the present implants severely limits widespread use of this clinically approved method.

To overcome these problems, a new implant system, based on inductive coupling principles, has been developed [(1),(17)]. It basically consists of two coils; there are no electronic components in the internal part of the system (Figure – 2); therefore, no breakdown due to component failure should be expected. So patients can use such a system along lifetime.

The new system is versatile and can be used to transmit any form of electro-therapeutic signals, including conventional stimulation and the experimental burst and frequency modulated stimulation patterns, that are known to be more effective in treating some clinical pain syndromes (Figure – 9), (Figure – 10) and (Figure – 11) [(18),(19),(20)].

The coils of the new system are small in size (active coil: 29 mm in diameter, 9 mm in height; passive coil: 21 mm in diameter, 6.5 mm in height) (Figure – 12); two or three of them could be used together to make a receiver coil array (Figure – 26) and (Figure – 27). The only thing the patient will do is to move the single transmitter coil over the receiver coil array to select the most effective channel of the multi-contact electrode. The coil arrays can facilitate the switching of the electrical stimulation

between a number of sites along the spinal column and thereby combat some of the difficulties of placement, targeting and accommodation.

The transmitter circuit of the new system has less number of electronic components than those of commercial devices, even than transcutaneous electrical nerve stimulators (TENS). It is, therefore, a cheaper and safer portable device providing three different modes of stimulation (conventional constant, burst and frequency modulation), which don't exist in most commercial devices. Because RF implants involve in a miniature radio wave transmitter, they have a complicated structure. The new transmitter, which contains less number of electronic components than that of even a TENS unit, is based on direct transmission of analog data (Figure – 4) and (Figure – 5).

In addition to solutions of the present problems of the existing system mentioned above, other advantages provided by the new implant system are as follows: The signal transmitted by the commercially-available radio-frequency dorsal column stimulators is mono-phasic in nature (Figure – 19) (Figure – 20) which means involment of direct current (DC). Electrolysis resulting from the polarity is a known factor to be considered. The pulse induced by the new system is a biphasic looking DC free signal (Figure – 16) and (Figure – 17) which is useful to minimize any undesirable electrolysis phenomena that may result in breakage in the lead and tissue necrosis (3).

All these factors reduce the cost of the new implant system, while conveying the additional advantages of safety and reliability. The new implant should prove more reliable than the existing systems because of its inherent simplicityWe can explain our innovation as follows: The device is essentially two electromagnetic coils - a transmitter coil and a receiver coil - through which the electrical signals for neurostimulation are transmitted by inductive coupling across the skin of the patient [(1),(17)]. The passive coil, that is implanted under the skin, is connected with the electrode in the epidural space of the spinal cord (Figure – 2). The active coil is placed on the skin overlying the passive coil (Figure – 3). Both coils are formed by wrapping 1100 turns of 42 S.W.G. (standart wire gauge) enammelled copper wire on special bobbins made from food grade acetal, delrin. The number of turns of active coil is 1100, and that of passive coil 1000. The bobbins are housed in a circular ferrite pot core. The prototype receiver coils were then encapsulated in a room-temperature-curing medical grade silicon elastomer having a wall thickness of about 2 mm. Therapeutic signals produced by a simple transmitter device, that has less number of components than even those of common TENS units, are directly transmitted to the patient without using radio waves (Figure – 4) and (Figure – 5).

While the use of magnetic coupling principles in numerous electromagnetical devices (e.g. transformers), electromagnetic coils housed in a ferrite pot core have not previously been used in neuroimplantation (21). There are implantable bone healing stimulators making use of rod shaped ferrite cores, but these systems are intended for the transmission of radio-frequency signals which is also common in transistor radio-circuits [(22),(23)].

Cardiac pace-maker implants operating with inductive coupling principles, which were developed by Abrams and his colleagues in 1960, and applied by Irish cardiologists Neligan and Malley in 1971, 1971) involves air cored coils which are bigger in size (55 mm in diameter) [(24),(25)]. A big implant is not surgically preferrable. In the new system, the coils are housed in a ferrite pot core; this does not only enhance the inductive coupling but, more importantly, allows a 79% reduction in size compared with the original cardiac pacemaker coils (Figure – 21) and (Figure – 24) (26). The new device incorporates a ferrite pot core for analogue transmission of data which facilitates miniaturisation and fabrication of multiple electrode systems.

It is known that the signal flowing in the high voltage energy transmission lines decays rapidly; therefore, no accidental induction under these lines can be expected. After all, to ensure the reliability of the system for patient's safety, a series of environmental tests close to an electricity mains, a microwave oven, a television, a high voltage transformer station, and under a high voltage energy transmission line of 66 kV were carried out. During these tests, neither any accidental induction nor any interference in the induced pulse patterns were observed (1).

During safety tests, he temperature depandancy of the resistance of the passive coils were also studied to see whether the induced signal would vary at body temperature. At room temperature (18 °C), resistance of the passive coil was measured as 128 Ω. The same coil was then put and kept in a water bath containing water of 37 °C, that is normal body temperature, for 15 minutes. After 15 minutes, resistance of the coil was 132°. The transmitter coil was then connected to the stimulator output and placed on the receiver coil in water bath. This test showed that slight increase in the resistance of passive coil at body temperature in accordance with the known principles of electrotechnics, did not make any difference in shape and amplitude of the induced pulse (Figure – 15) and (Figure – 18) (1).

Silicones are widely used in the medical device industry. Adhesive silicone rubbers in particular have been shown to be suitable for the encapsulation of implantable medical electronic devices because of their good adhesive properties which yield a strong and durable seal (29). The encapsulation of an implant by a medical grade silicone rubber can be achieved by means of a simple mould. The optimum shape chosen for the implantable coil, however, should take into account those factors which may affect both the quality of the electrical coupling in addition to the surgical requirement that the device be compact. A fringe made from 0.5 mm medical grade silicone sheet (501-3, Dow Corning) was used on the base of the receiver coil to suture it under the skin, thus avoiding any unwanted movement after the operation (Figure 26) and (Figure – 27).

Industrial Application of the New Implant System:

A workshop having electronics, biomaterials, storage room and administration rooms is needed to manufacture the new implant. Gamma radiation technics is suitable for sterilisation of the implantable parts of the system (passive coil and electrodes). Medical application must be undertaken by a professional center employing at least a neurosurgeon, an anesthesiologist, a cardiologist and physical therapy specialist who are particularly trained in the field of neurostimulation and neuroimplantation. Direct marketing of such a device to patients and physicians is not correct. Only above mentioned medical centers with appreciated qualifications must be authorized to purchase these devices.

CLAİMS

1) An externally activated neuro-implant which directly transmits therapeutic signals, specified as followings: It is an implantable device carrying out electrical stimulation of the nerves system. It basically consists of two coils; there are no electronic components in the internal part of the system. The passive coil, that is implanted under the skin, is connected with the electrode in the epidural space of the spinal cord. The active coil is placed on the skin overlying the passive coil. Therapeutic signals produced by the transmitter outside the body are directly transmitted by inductive coupling across the skin of the patient [(1),(17)].

2) The innovation mentioned in requirement 1, specified as followings: Both coils are formed by wrapping 42 S.W.G. (standart wire gauge) enammelled copper wire on special bobbins made from food grade acetal, delrin. The number of turns of active coil is 1100, and that of passive coil 1000. The bobbins are housed in a circular ferrite pot core. The transmitter that has less number of components than even those of common TENS units. Direct transmission of analog data is carried out without using radio waves.

3) The innovation mentioned in requirement 1, specified as followings: It is known that the signal flowing in the high voltage energy transmission lines decays rapidly (27). After all, to ensure the reliability of the system for patient's safety, a series of environmental tests close to an electricity mains, a microwave oven, a television, a high voltage transformer station, and under a high voltage energy transmission line of 66 kV were carried out, and neither any accidental induction nor any interference in the induced pulse patterns were observed (1).

4) The innovation mentioned in requirement 1, specified as followings: Silicones are widely used in the medical device industry. Adhesive silicone rubbers in particular have been shown to be suitable for the encapsulation of implantable medical electronic devices because of their good adhesive properties which yield a strong and durable seal (29). The encapsulation of an implant by a medical grade silicone rubber can be achieved by means of a suitable mould. The optimum shape chosen for the implantable coil, however, should take into account those factors which may affect both the quality of the electrical coupling in addition to the surgical requirement that the device be compact. A fringe made from 0.5 mm medical grade silicone sheet (501-3, Dow Corning) was used on the base of the receiver coil to suture it under the skin, thus avoiding any unwanted movement after the operation.

5) The innovation mentioned in requirement 1, specified as followings: Transmitter of the new system provides any form of electro-therapeutic signals, including conventional stimulation and the experimental burst and frequency modulated stimulation patterns [(18),(19),(20)].

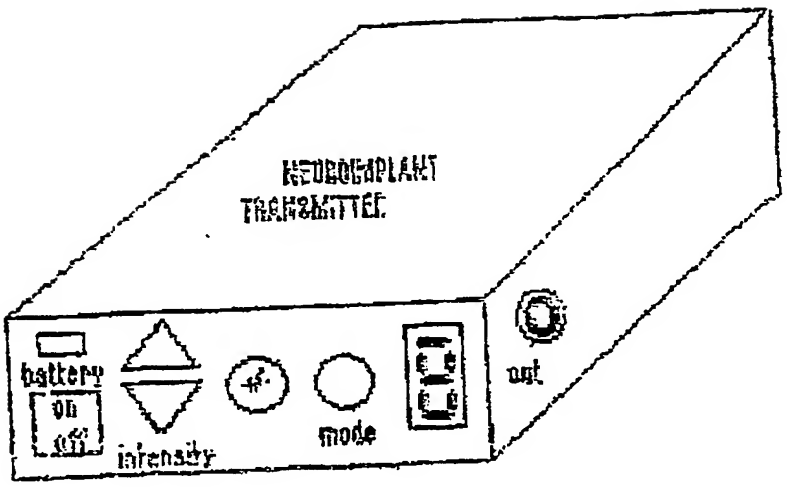
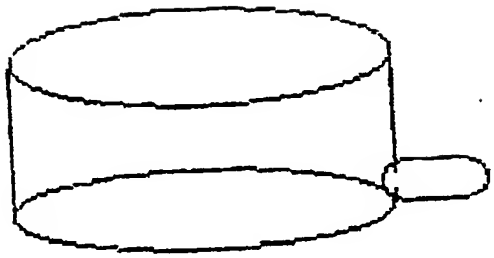


Figure 1



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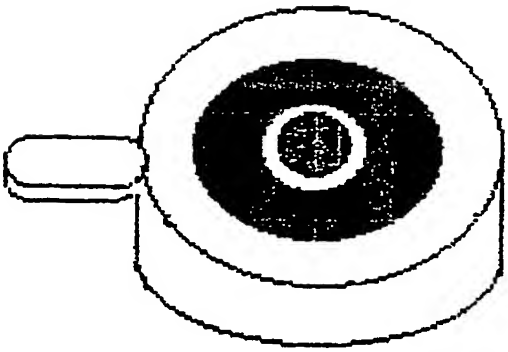

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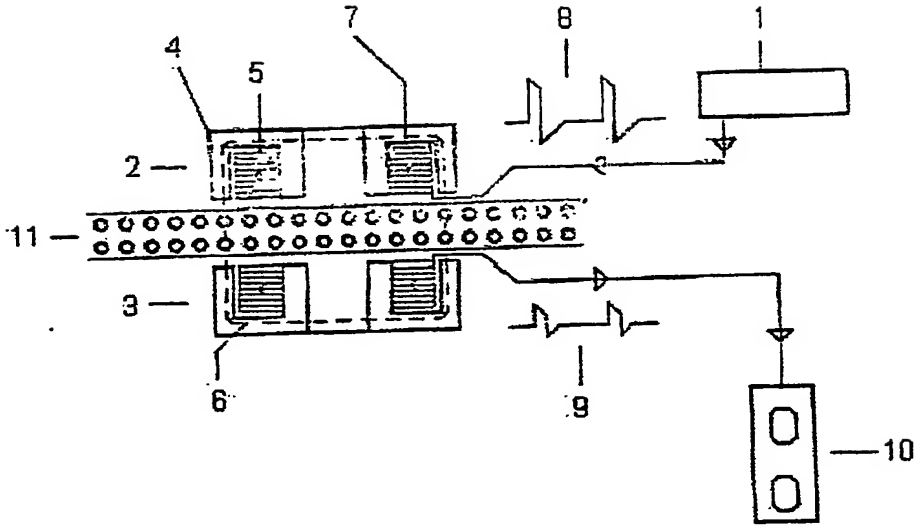

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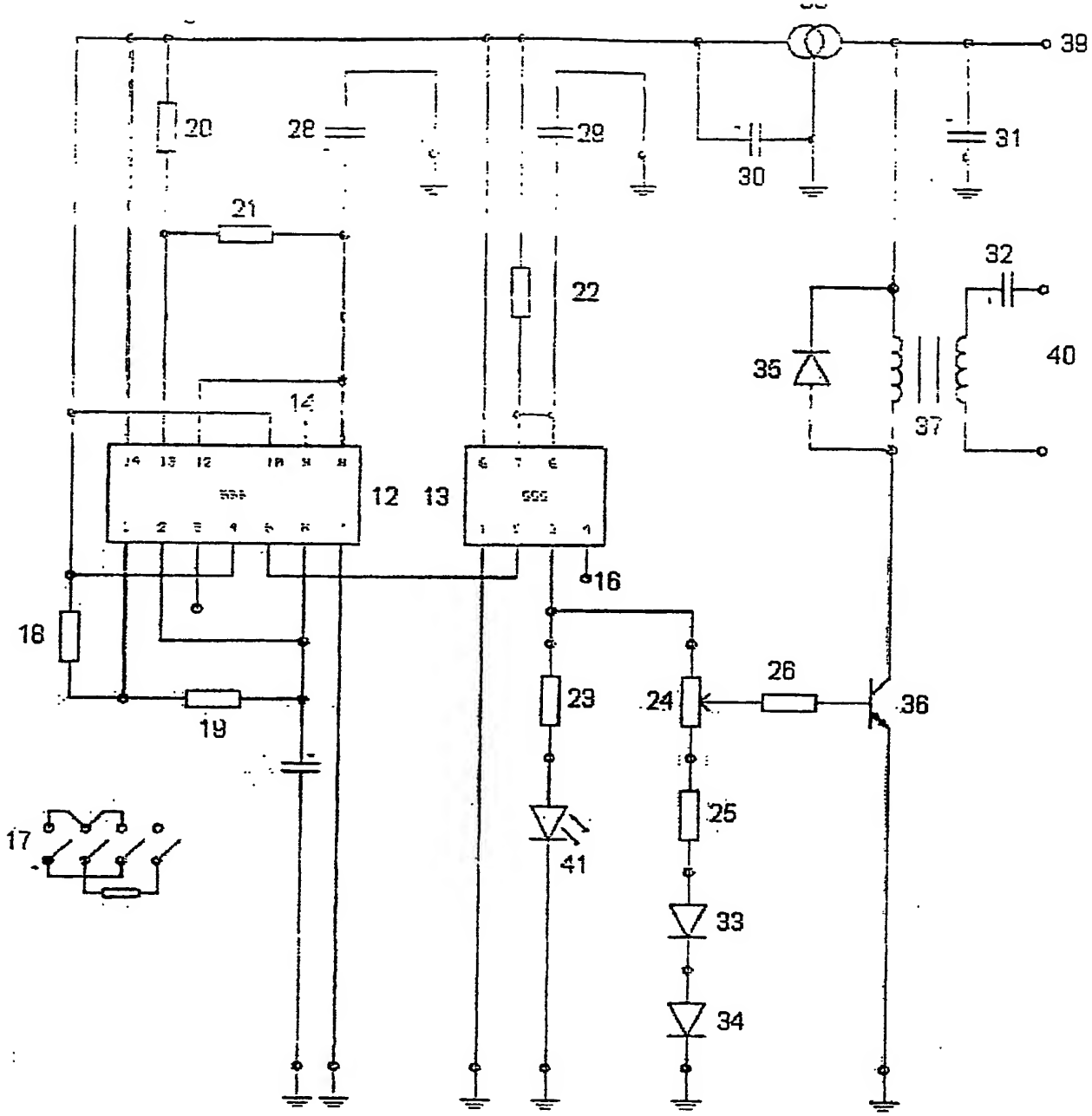
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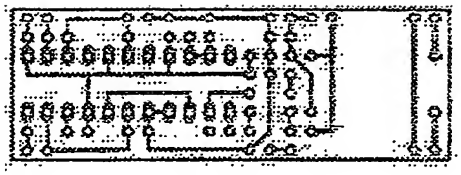
Figure - 5



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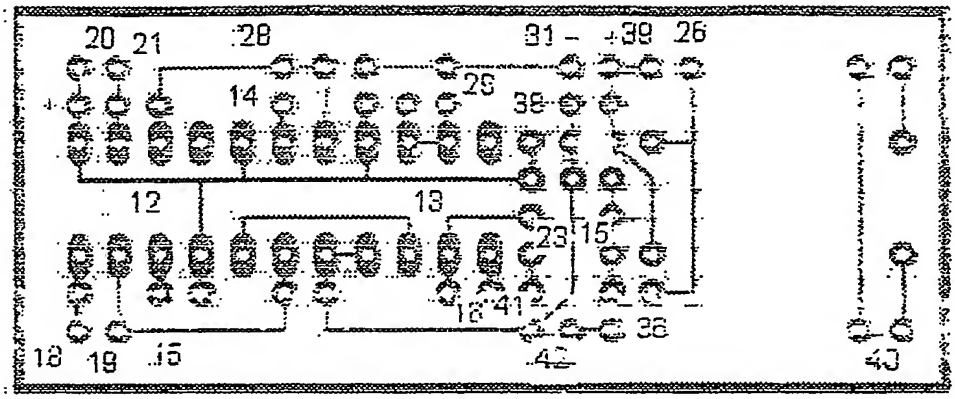

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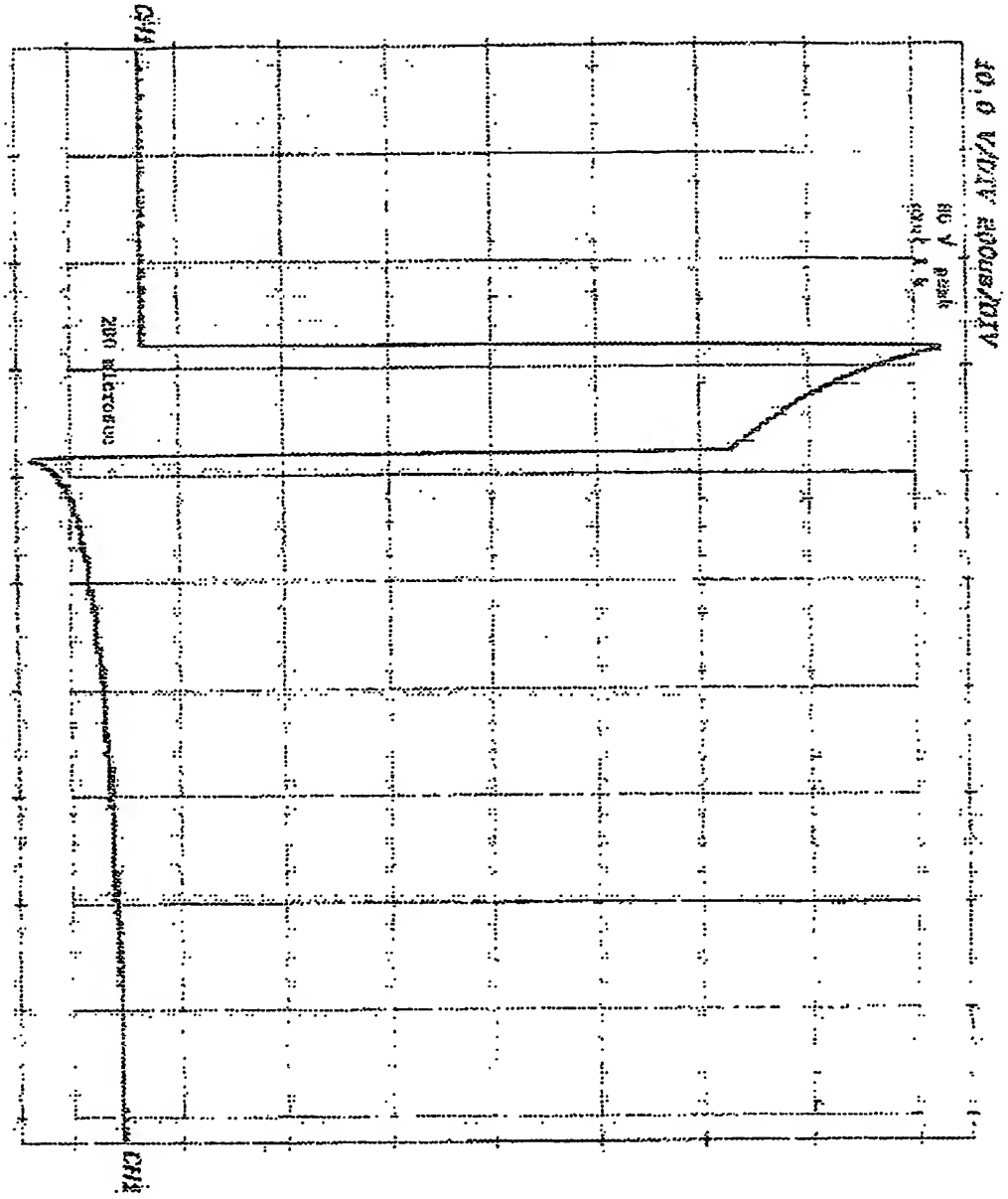

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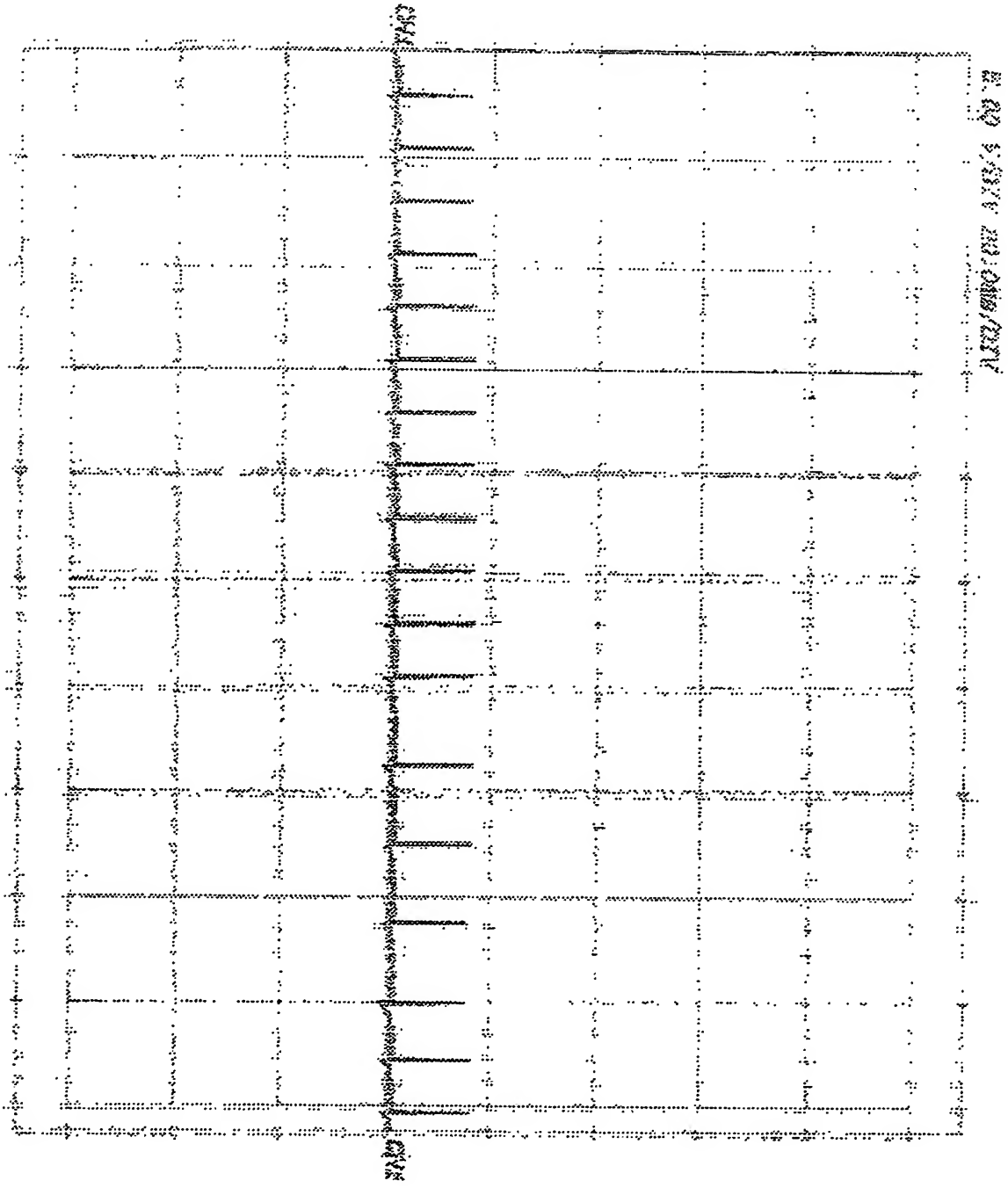


Figure - 9

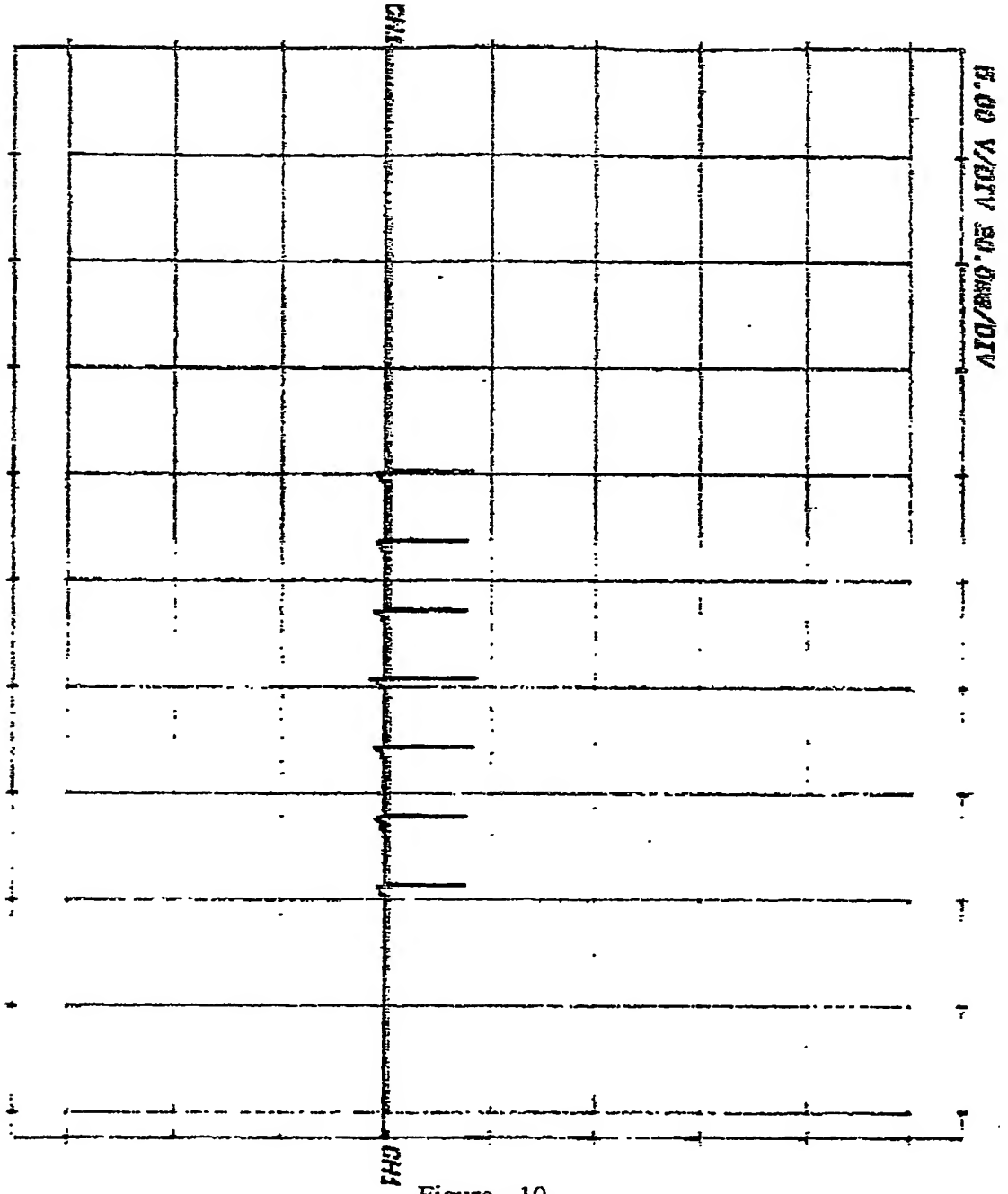
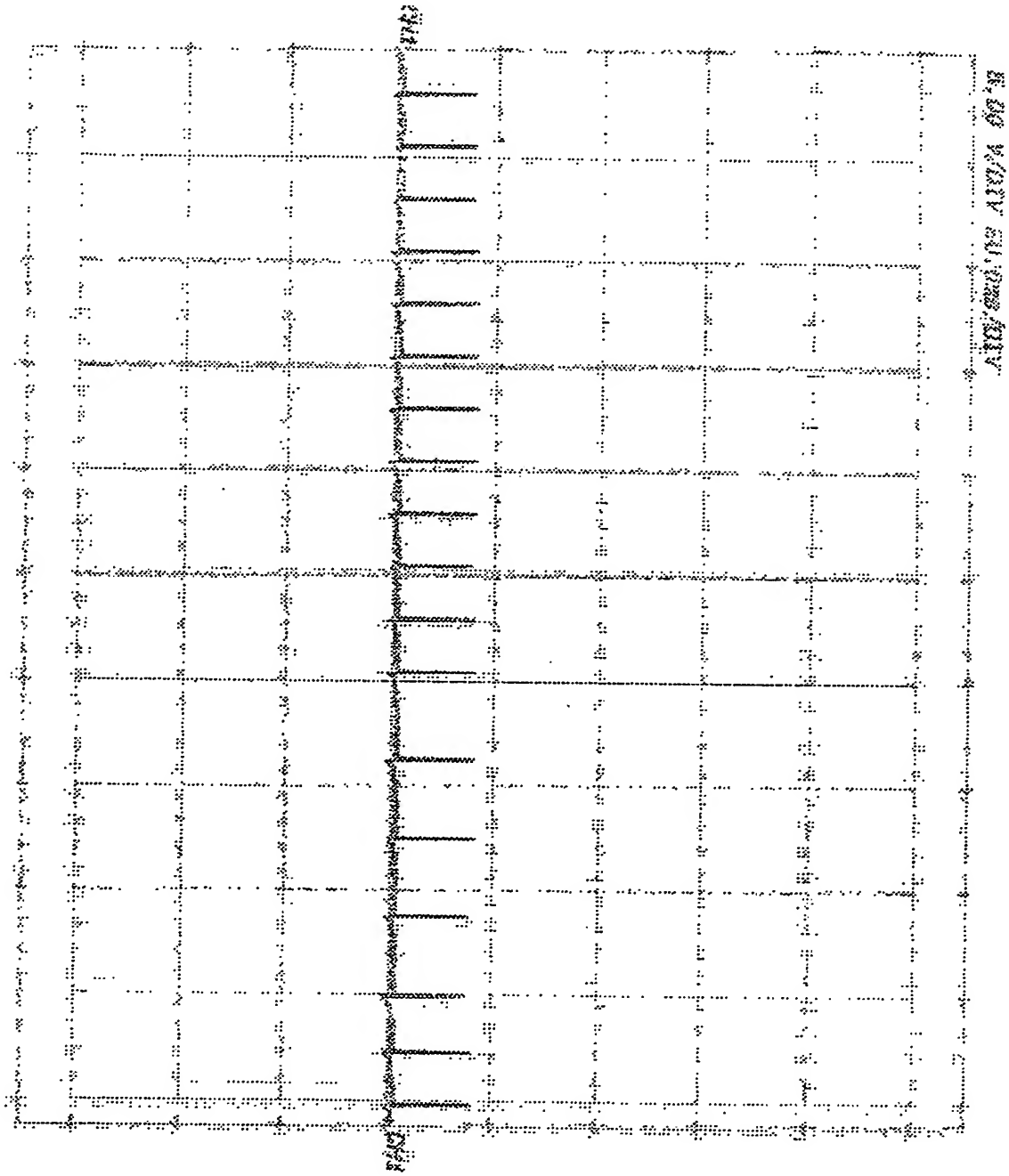


Figure - 10



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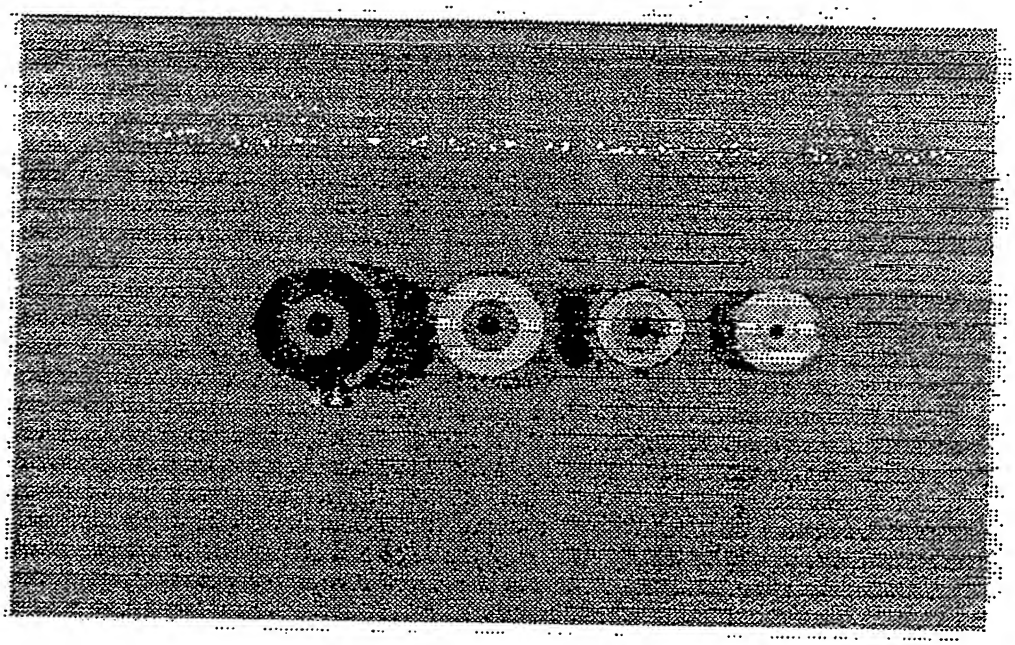

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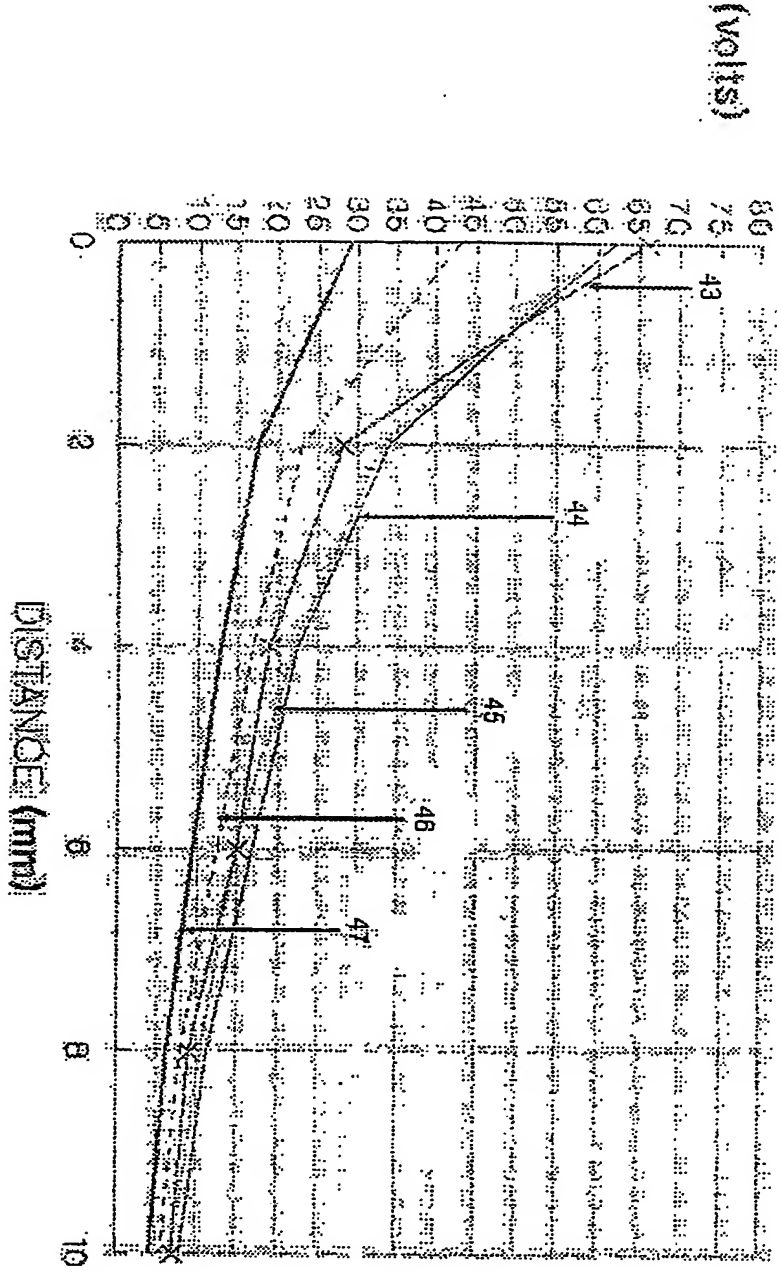

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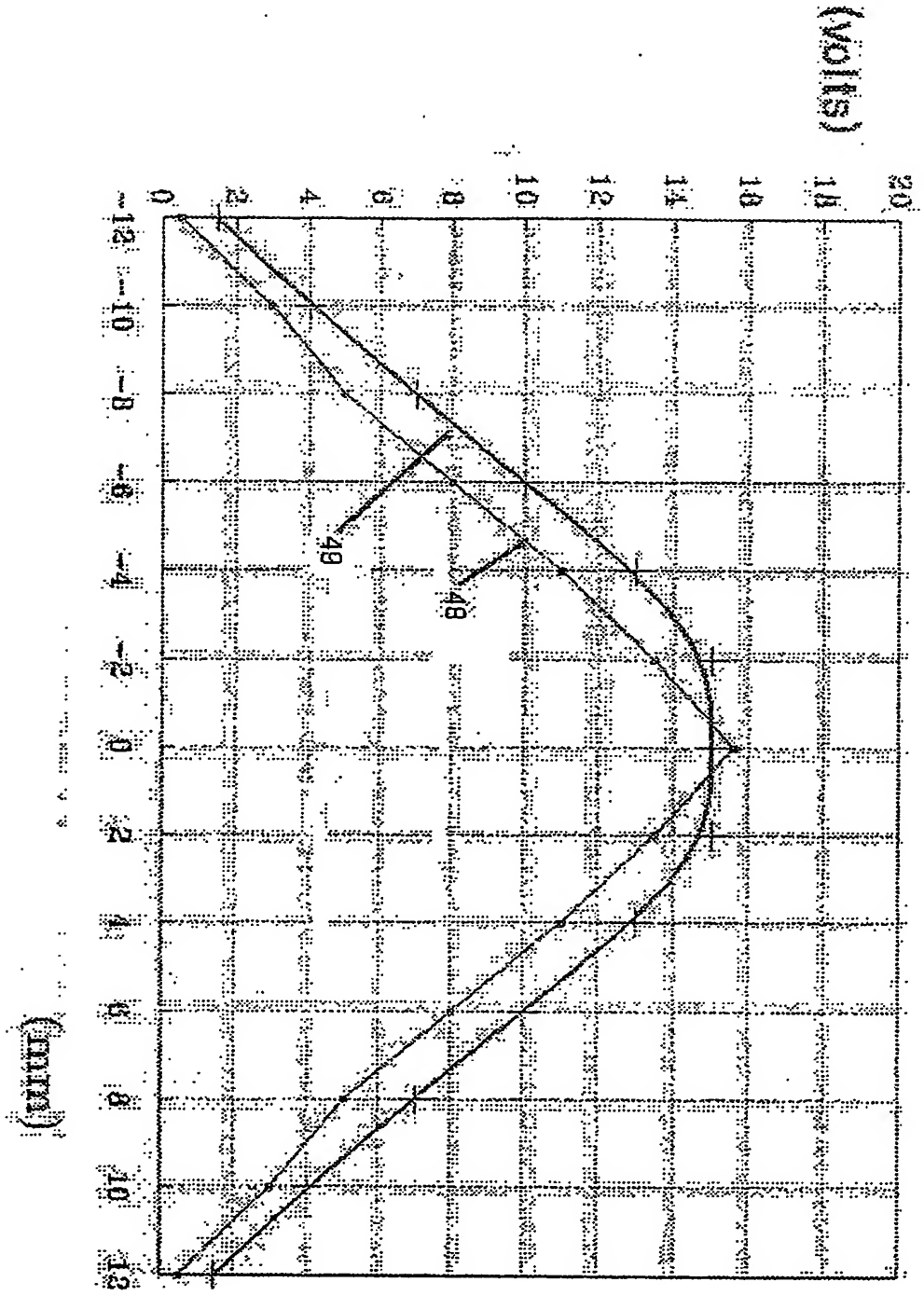

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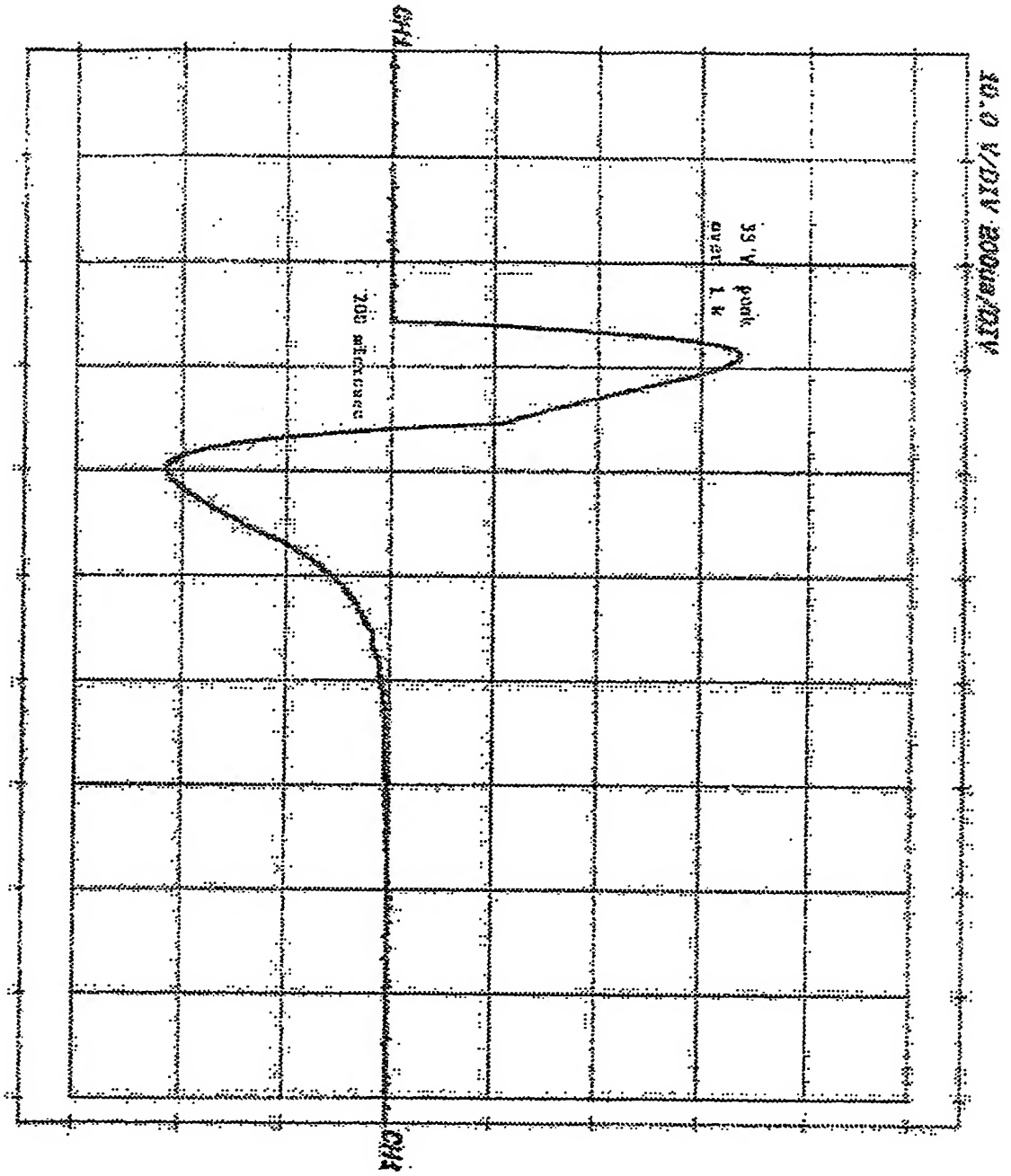

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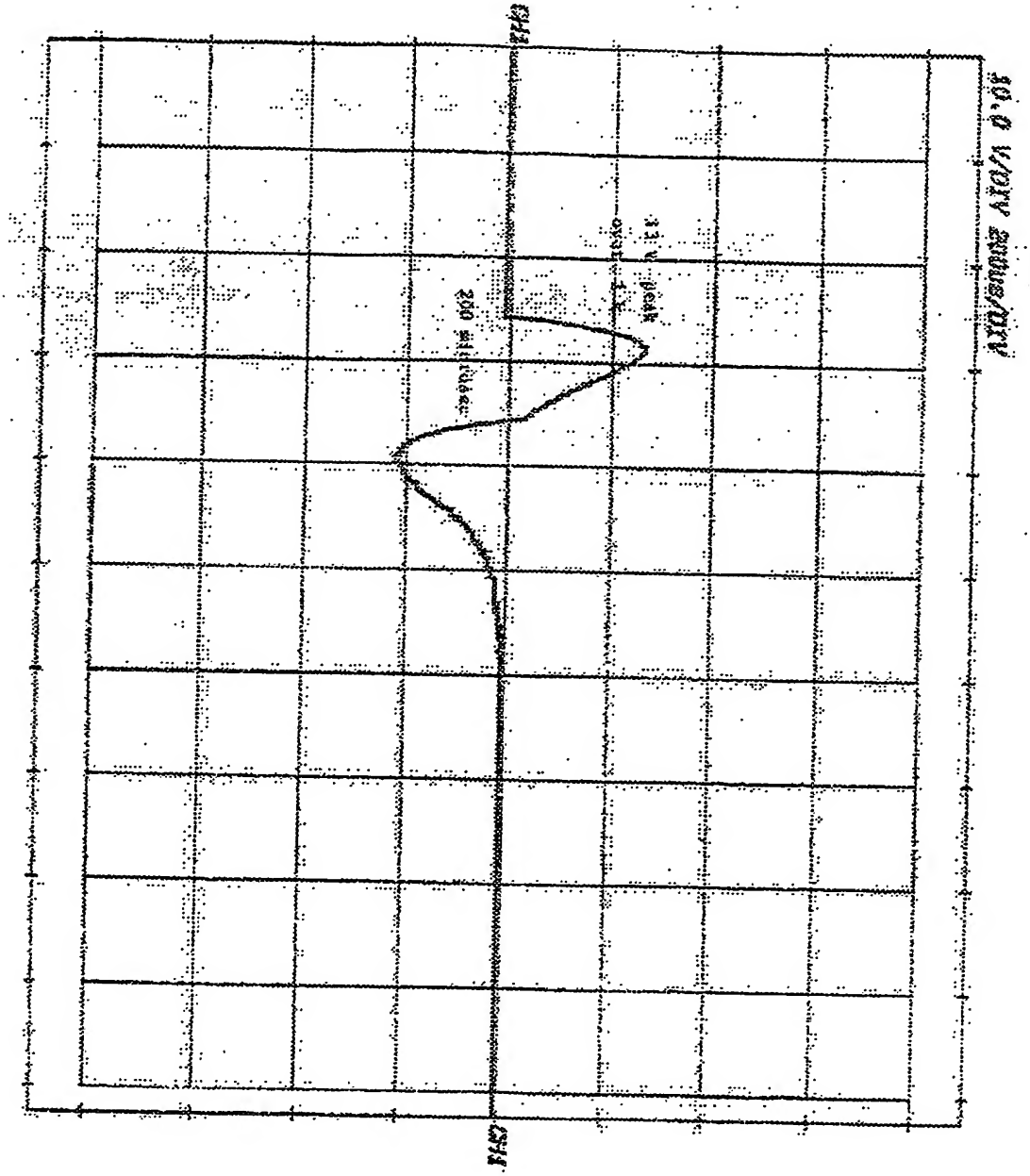

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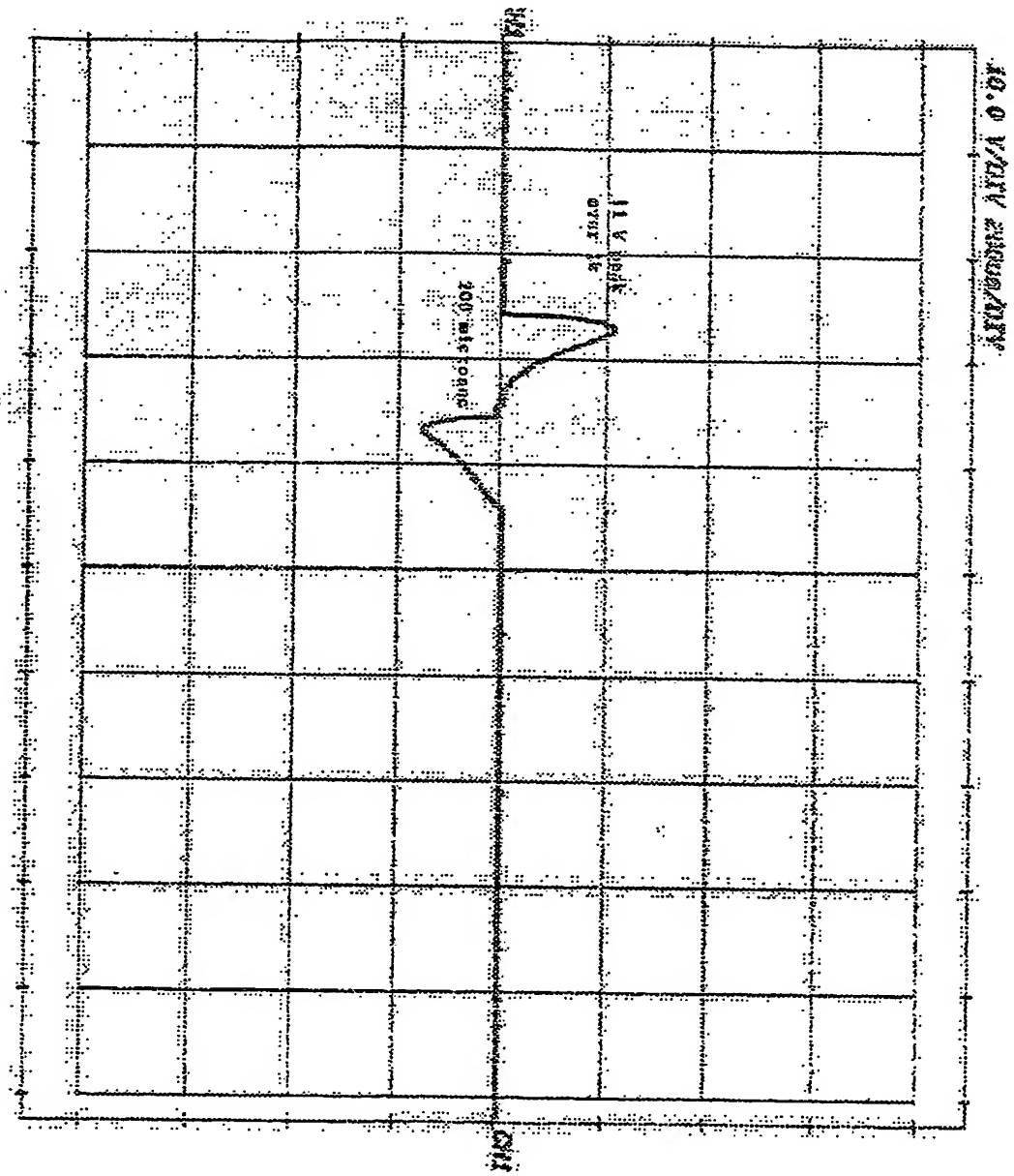

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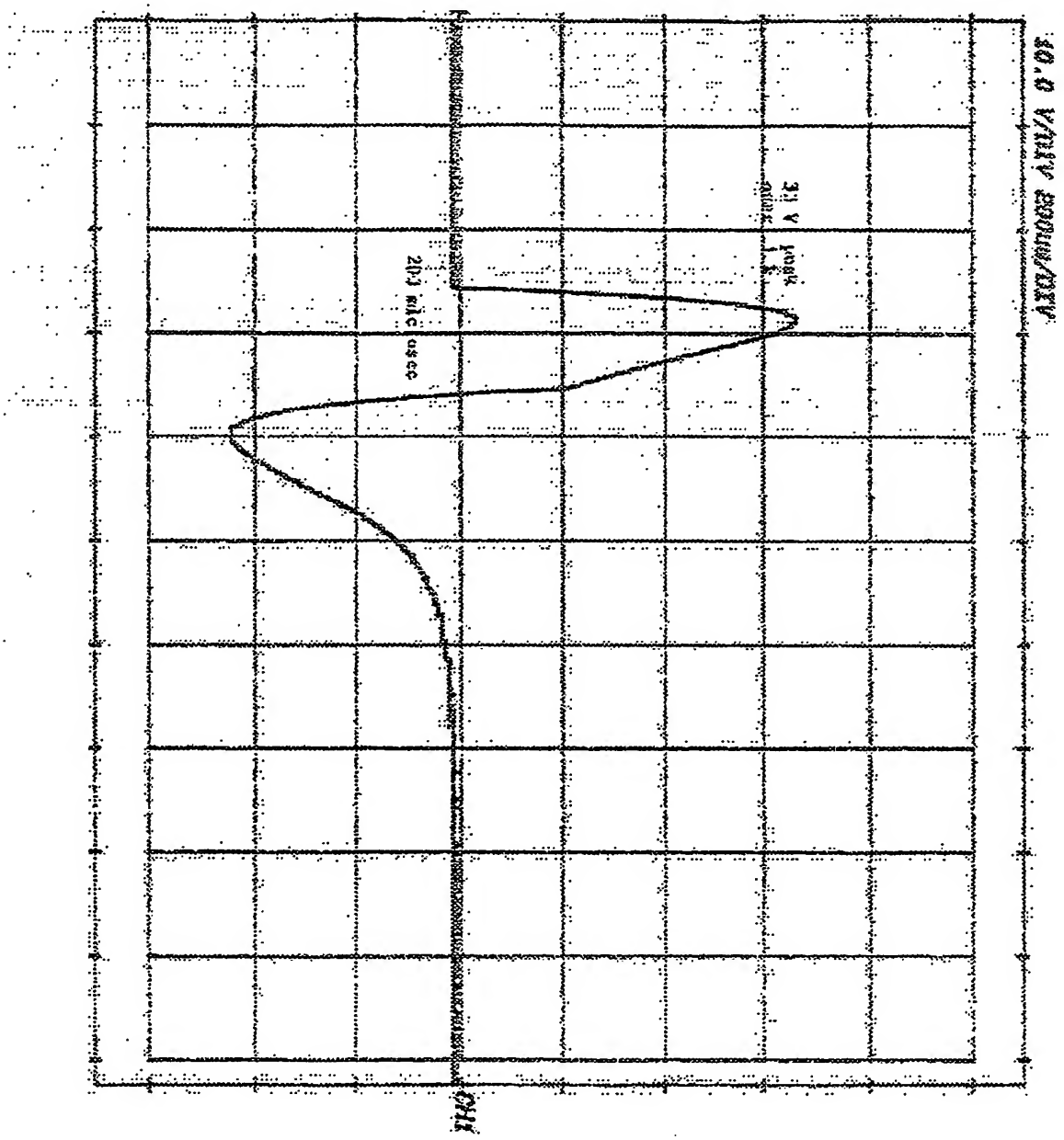

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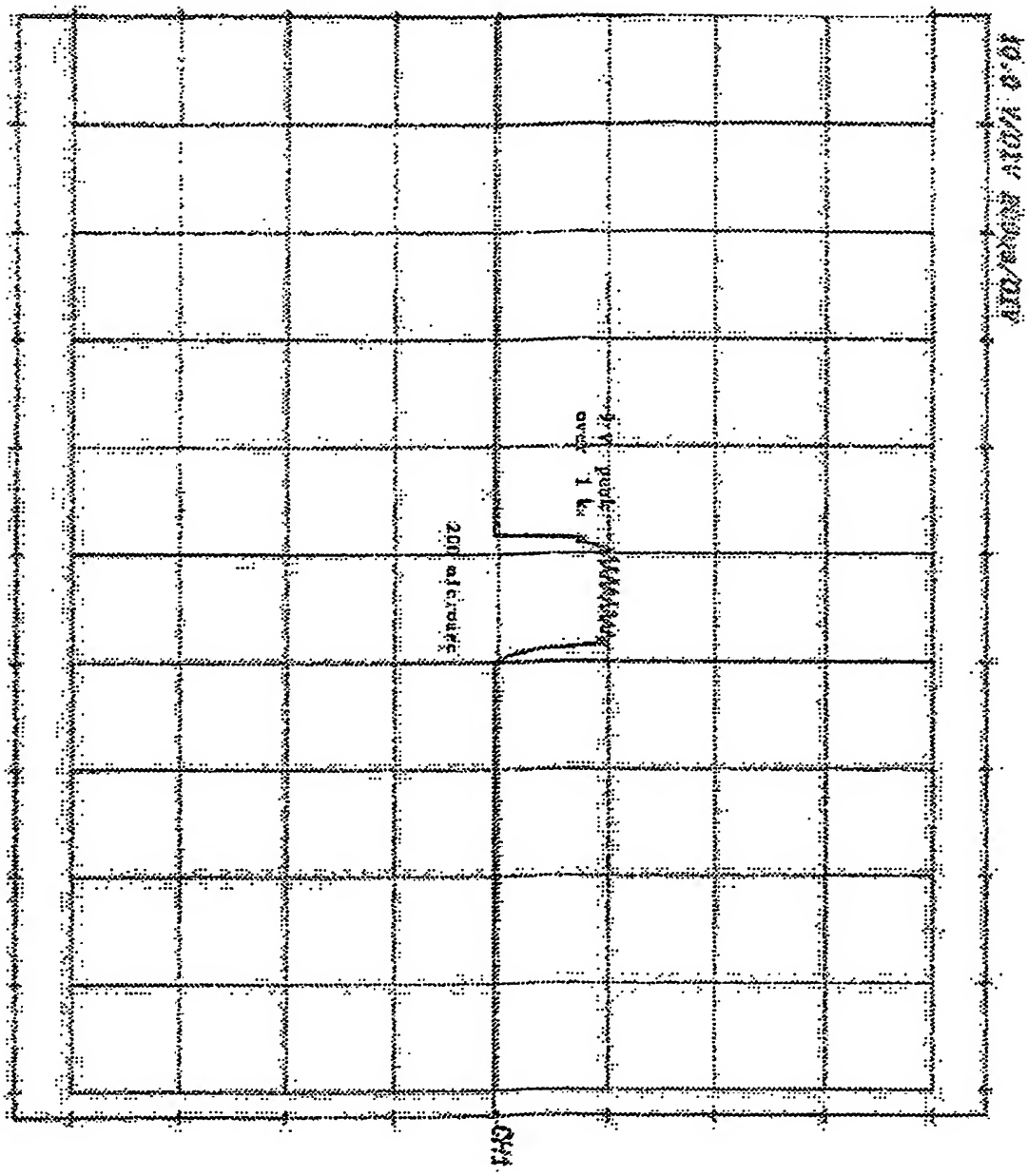

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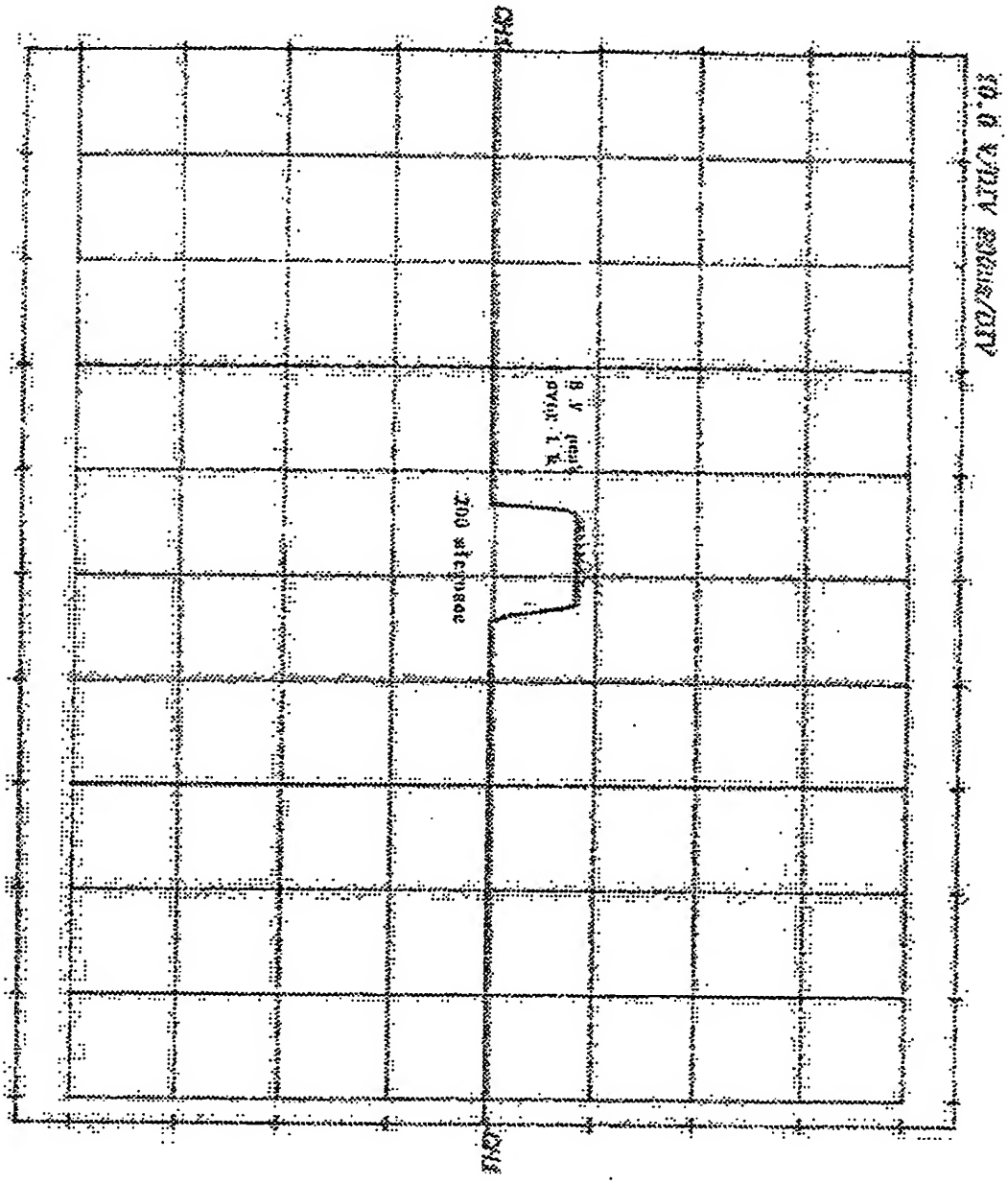

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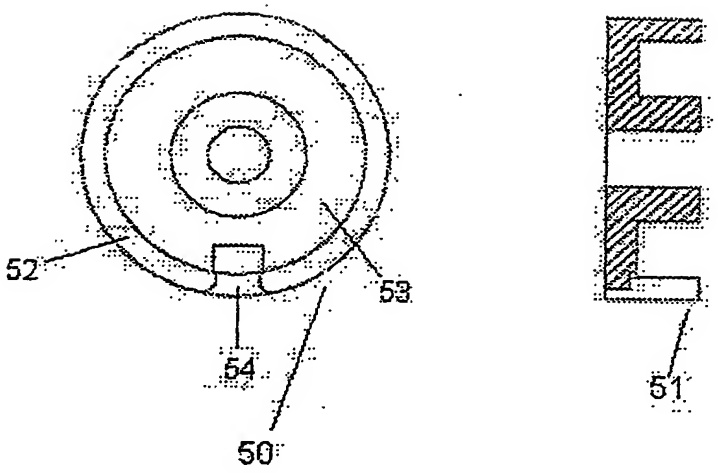

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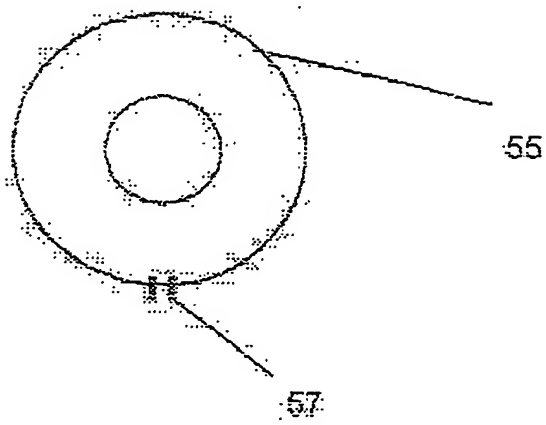

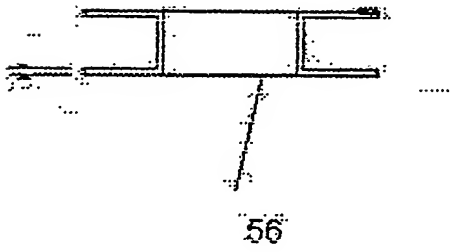

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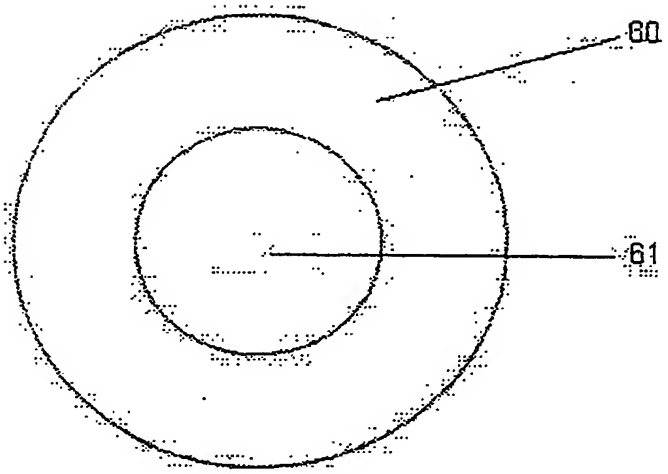

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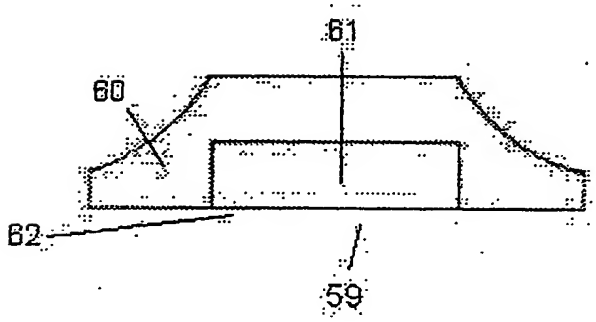

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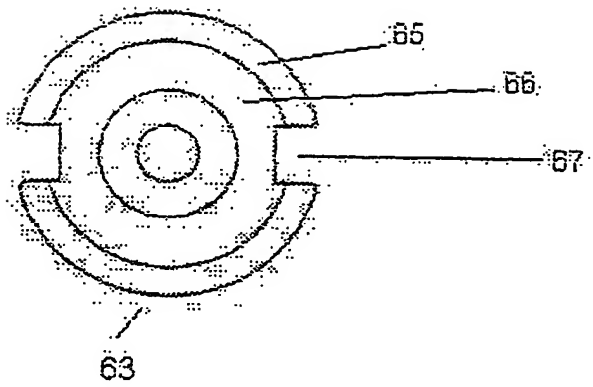

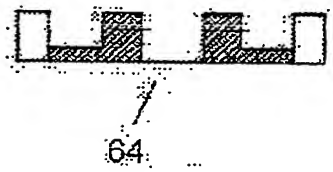

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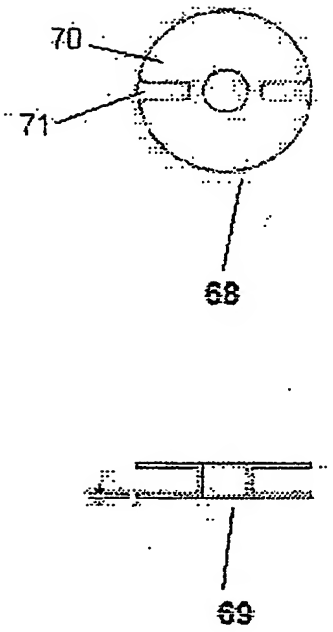

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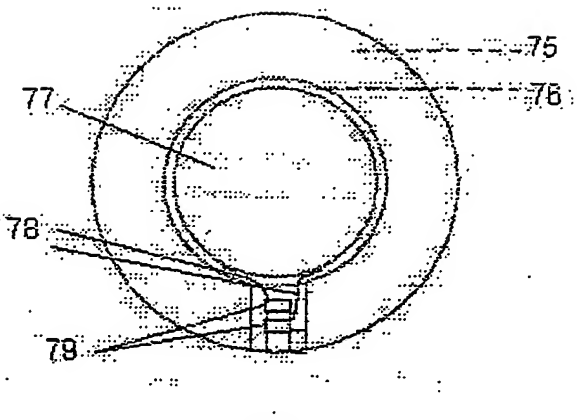

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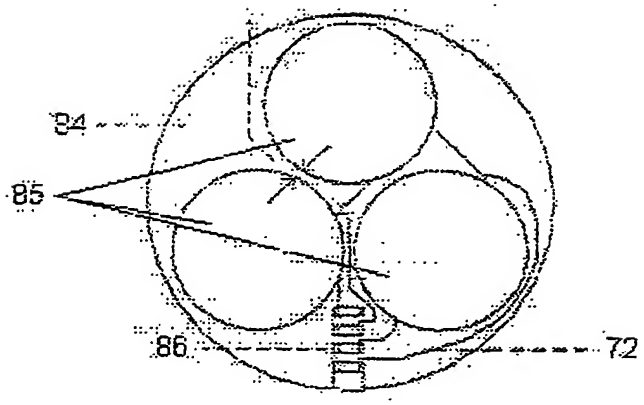

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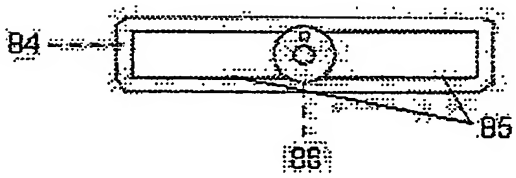

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Figure - 27

INTERNATIONAL SEARCH REPORT

Int[redacted]al Application No
PC[redacted]R 03/00092

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N1/36 A61N1/37 A61N1/368 A61N1/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y A	US 5 070 535 A (HOCHMAIR INGEBORG J ET AL) 3 December 1991 (1991-12-03) column 2, line 14 -column 2, line 62; claim 1	1 2-5
Y	US 4 741 339 A (HARRISON JAMES M ET AL) 3 May 1988 (1988-05-03) abstract; claim 1	1
Y	US 6 088 619 A (HEIN WALTER ET AL) 11 July 2000 (2000-07-11) the whole document	1
Y	EP 1 166 820 A (MEDTRONIC INC) 2 January 2002 (2002-01-02) paragraphs '0001!-'0004!; figure 1	1

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
11 May 2004	18/05/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Chopinaud, M

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Int[redacted]al Application No
PC[redacted]R 03/00092

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 493 587 B1 (BECKER MICHAEL ET AL) 10 December 2002 (2002-12-10) abstract; claim 1	1-5
A	US 4 361 153 A (SLOCUM CHESTER D ET AL) 30 November 1982 (1982-11-30) column 5, line 36 -column 8, line 16	1-5

[redacted]mation on patent family members

Intd [redacted]al Application No
PCT/FR 03/00092

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 5070535 A	03-12-1991	AU	5481786 A	25-09-1986
		CA	1276240 C	13-11-1990
		EP	0200321 A2	05-11-1986
		JP	61276568 A	06-12-1986
US 4741339 A	03-05-1988	CA	1246680 A1	13-12-1988
		EP	0179536 A2	30-04-1986
US 6088619 A	11-07-2000	DE	19908438 A1	21-09-2000
		EP	1032109 A2	30-08-2000
EP 1166820 A	02-01-2002	EP	1166820 A2	02-01-2002
US 6493587 B1	10-12-2002	DE	19962915 A1	06-09-2001
		AU	6823100 A	09-07-2001
		CA	2395495 A1	05-07-2001
		WO	0147598 A1	05-07-2001
		EP	1307258 A1	07-05-2003
		TW	542712 B	21-07-2003
US 4361153 A	30-11-1982	US	4494545 A	22-01-1985